

2. (amended) The method of claim 1, wherein the Fyb/SLAP complex inhibitor binds to the EVH1 domain of the Ena/VASP protein and inhibits binding of the Ena/VASP protein to a Fyb/SLAP protein.

### **REMARKS**

Claims 1, 2, 4, 26, 30, 39, 42, and 73-83 are pending. Claim 1 has been amended to clarify the meaning of cell and cell fragment and claim 2 has been amended as suggested by the Examiner to correct the typographical error in the claim. No new matter has been added.

### **Informalities**

Applicants have amended claim 2 to remove the word "the" that was inadvertently duplicated in the claim as filed.

### **Drawing Informalities**

Although the drawings submitted by Applicants with the Application as filed were informal drawings, Paper 11, paragraphs 12 and 13 indicate that the drawings failed to comply with CFR 1.84 and require that corrected drawings be filed. Applicants have now filed formal, corrected drawings with the Drawing Review Branch as indicated on the Notice of Draftsperson's Patent Drawing Review that was included in Paper No.:11. For the Examiner's convenience, Applicants include herewith a copy of the drawings as filed with the Drawing Review Branch.

### **Rejections Under 35 U.S.C. §112, Second Paragraph**

The Examiner rejected claims 1, 2, 4, and 73-77 under 35 U.S.C §112 as being indefinite for failing to particularly point out and distinctly claim the invention and asserts that the meaning of the term "cell fragment" with regard to the claimed invention is unclear.

Applicants submit that the amendment to claim 1, to include the characterization of the cell or cell fragment as comprising Fyb/SLAP and Ena/VASP proteins that form a complex also addresses the rejection of the claim as indefinite under 35 U.S.C §112. Applicants submit that meaning of the term "fragment" is that commonly understood to be "a part broken off or

detached” (The Merriam-Webster Dictionary, page 303, Merriam-Webster Incorporated, Springfield, MA, 1997). Thus, a cell fragment of claim 1, would be understood by one of ordinary skill in the art to be a part of a cell that comprises Fyb/SLAP and Ena/VASP proteins that form a complex. Applicants submit that claim as amended is not indefinite and respectfully request that the Examiner withdraw the rejection under 35 U.S.C. §112.

### **Rejections Under 35 U.S.C. §112, First Paragraph**

#### **Enablement**

The Examiner rejected claims 1, 2, 4, 26, 30, 39, 42, and 73-83 as lacking enablement under 35 U.S.C. §112. The Examiner states that the specification is enabling for a method for inhibiting cytoskeletal rearrangement in a T cell or a platelet, a method for inhibiting a T cell response and a method for increasing platelet aggregation comprising contacting the T cell or platelet with an amount of a Fyb/SLAP complex inhibitor sufficient to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein wherein the Fyb /SLAP inhibitor is EVH1 binding peptide FPPPP (SEQ ID NO:15), but contends that the specification is not enabling for “any cell or cell fragment” in claim 1. Applicants have amended claim 1 to clarify that the cell or cell fragment is a cell or cell fragment comprising Fyb/SLAP and Ena/VASP proteins that form a complex. Applicants respectfully submit that this amendment to claim 1, obviates the basis for the Examiner’s rejection based on the scope of the claims.

The Examiner also asserts that Applicant has not provided sufficient information regarding the identity of Fyb/SLAP complex inhibitors, inhibitors that bind to the EVH1 domain or peptide mimetic other than the proline rich peptide FPPPP (SEQ ID NO:15). Applicants respectfully submit that Applicants are not claiming specific inhibitory agents, but rather are claiming methods of using such agents. Applicants further assert that the specification and Examples provide adequate guidance as to how the skilled artisan can identify potential inhibitory agents and determine their binding characteristics and effects, and thus use such agents in the claimed methods.

Applicants submit that methods of testing the ability of putative inhibitors to inhibit Fyb/SLAP binding to Ena/VASP are described both in Example 3, and also on page 32, line 3 through page 36 line 3, which provide an extensive description of various methods to determine

the ability of an agent to inhibit binding between Fyb/SLAP and Ena/VASP proteins. Applicants submit that given these descriptions regarding how to make, identify, test, and use inhibitory agents, and given the fact that making antibodies and peptide mimetics is considered a routine procedure in the art, one of ordinary skill would find more than adequate guidance in the application as filed as to how to make and use a Fyb/SLAP complex inhibitor.

Taking into consideration the Examiner's statements with respect to the requirement to perform undue experimentation to practice the invention, Applicants maintain that the claimed invention is enabled based on an analysis of all of the eight Wands factors. Although some of these factors (scope of the claims, guidance presented, sufficient working examples, and unpredictability in the art) were considered by the Examiner; all of the factors should be considered for a proper analysis and a finding of nonenablement must be based on the evidence as a whole. In re Wands 858 F.2d 731, 737, 740, 8 U.S.P.Q.2d 1400, 1404, 1407 (Fed. Cir. 1988). Applicants maintain that full consideration of all of the Wands factors, in view of the state of the art at the time of filing, leads one to the reasonable conclusion that practicing the invention would not require undue experimentation.

The Examiner has considered the guidance presented and concluded that undue experimentation would be required for one of ordinary skill in the art to practice the invention. Applicants respectfully traverse the rejection on the grounds that Applicants provide definitions, use commonly accepted terms in the claims, and also provide guidance in the Specification and in the form of examples, including strategies to make and identify putative inhibitory agents. For example, page 26, line 28 through page 29, line 19 describes making antibodies, and page 8, lines 22-23 provides a description of how one would identify a peptide mimetic of the invention. This latter description teaches that a peptide mimetic would be a mimetic having an equivalent binding specificity to FPPPP (SEQ ID NO:15) and that "equivalent binding specificity" means that the mimetic competes for binding with the peptide FPPPP (SEQ ID NO:15)." Applicants assert that one of ordinary skill would recognize that an antibody or mimetic that interferes with binding between Fyb/SLAP and Ena/VASP would qualify as an inhibitory agent in the claimed invention.

Additionally, Applicants assert that the specification and examples teach assays that one of ordinary skill in the art would be able to use to determine the inhibitory characteristics and

effects of putative inhibitory agents on the binding of Fyb/SLAP and Ena/VASP proteins. Applicants submit that methods of testing the ability of putative inhibitors of binding between Fyb/SLAP and Ena/VASP proteins are described both in Example 3, and also on page 32, line 3 through page 36 line 3, which provides an extensive description of various methods of determining inhibition of binding by an agent, including antibodies and mimetics useful in practicing the invention. Applicants assert that given these descriptions regarding how to make, identify, test, and use the inhibitor agents of the invention, and given the fact that making antibodies and peptide mimetics is considered a routine procedure in the art, one of ordinary skill would find more than adequate guidance as to how to make and use a Fyb/SLAP complex inhibitor.

The specific definitions of the claim terms along with the examples provide guidance to one of ordinary skill in the art on how to make and identify antibodies and mimetics that inhibit binding of Fyb/SLAP with Ena/VASP. Thus, the guidance presented is not only by itself an insufficient reason to find a lack of enablement as a result of undue experimentation for practicing the claimed invention, the guidance presented in fact favors a finding of enablement.

The Examiner also refers to the following Wands factors: 1) scope of the claims, 2) predictability of the art, 3) quantity of experimentation, and 4) working examples. As described above, Applicants submit that the amendment to claim 1, to more clearly define the scope of the claimed invention, obviates “scope of the claims” as a basis for an enablement rejection. In addition, Applicants respectfully submit that none of the other three factors would weigh against a finding of enablement for the claimed invention.

Applicants respectfully assert that the Examiner’s argument regarding unpredictability of protein folding and tertiary structure is not germane to issue of the enablement of the claimed invention. As described herein, the Specification and Examples provide extensive teaching regarding how one of ordinary skill would be able to identify and test agents for their ability to inhibit binding of Fyb/SLAP and Ena/VASP. Applicants point out that a prediction of the three-dimensional structure of any of these putative agents would not be necessary for the determination of their inhibitory abilities. Antibodies made against either Fyb/SLAP or Ena/VASP proteins can be assayed as described in the instant application without any prediction of three-dimensional structure or how structure relates to function. With respect to the

identification of peptide mimetics, Applicants submit that one of ordinary skill would simply use routine strategies to modify peptides such as FPPPP (SEQ ID NO:15), and then test the resulting peptides to determine their ability to inhibit binding of Fyb/SLAP and Ena/VASP proteins. Applicants assert that the relationship between the structure and function of these putative binding agents need not be predicted and that one of ordinary skill in the art can reliably make and test the antibodies and mimetics for use in the claimed invention, particularly given the disclosure in the specification.

The Examiner additionally states that “minor structural differences among structurally related compounds or compositions can result in substantially different biological activities” (Paper 11, Page 4, final paragraph). Applicants agree the statement is true, but contend that it does not provide grounds for an enablement rejection. Claim 1 states that a cell or cell fragment comprising Fyb/SLAP and Ena/VASP proteins that form a complex is contacted with an amount of a Fyb/SLAP complex inhibitor “sufficient to inhibit,” binding between Fyb/SLAP and Ena/VASP proteins. Thus, one of ordinary skill in the art would use an assay such as those provided in the application to ascertain whether or not a putative inhibitor is in fact inhibitory, and determine the amount of that inhibitor that is sufficient to inhibit the binding of Fyb/SLAP and Ena/VASP proteins. Applicants submit that sufficient direction has been provided for one of ordinary skill in the art to make and use an agent that inhibits binding of Fyb/SLAP and Ena/VASP proteins and can also readily utilize the provided assays to determine an effective amount of an inhibitor.

The final two Wands factors are crucial to any determination of undue experimentation. In the Wands case, for example, the court’s decision turned on the “high level of skill in the art at the time the application was filed”, and that “all of the methods needed to practice the invention were known.” Wands at 740, 8 U.S.P.Q.2d at 1406. Applicants maintain that the same conclusions with respect to the state of the art and the level of skill in the art are true in the instant case, and therefore must weigh heavily in favor of a finding that undue experimentation is not required.

The level of skill in the art has an important effect on the amount of guidance which must be provided to enable the invention. As the court stated in In re Howarth, “[i]n exchange for the patent, [the applicant] must enable others to practice his invention. An inventor need not,

however, explain every detail since he is speaking to those skilled in the art.” In re Howarth, 654 F.2d 103, 105 (C.C.P.A. 1981). Thus the level of knowledge of one of ordinary skill in the art cannot be ignored in the Wands factor analysis. For the standard procedures contemplated in the application, the level of skill in the art is high. Applicants maintain that the person of ordinary skill in the art of cell biology would know how to prepare, test, and use agents that inhibit binding between Fyb/SLAP and EnaVASP in the claimed methods, given the guidance presented in the application as filed. Accordingly, Applicants assert that they have enabled the claims throughout their scope and respectfully request that the Examiner withdraw the rejection of claims 1, 2, 4, 26, 30, 39, 42, and 73-83 under 35 U.S.C. §112, first paragraph.

#### Written Description

The Examiner rejected claims 1, 2, 4, 26, 30, 39, 42, and 73-83 under 35 U.S.C. §112, first paragraph as lacking adequate description. Applicants have amended claim 1, as described above, and believe this clarifies that Applicants were in possession of the claimed methods.

The basic requirement of the written description requirement is that the claimed invention must be described clearly enough to allow one of ordinary skill in the art to recognize that the inventors invented the claimed invention. Vas-Cath v. Mahurkar 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991); Lockwood v. American Airlines, Inc. 107 F.3d 1565, 41 USPQ2d 1961 (Fed. Cir. 1997); In re Gosteli 872 F.2d 1008, 10 USPQ 2d 1614 (Fed. Cir. 1989). The requirement is based on the knowledge of the skilled artisan in the particular art: the applicant must convey to one of ordinary skill in the art through the disclosure in the invention that the applicant was in possession of the claimed invention.

In the instant case, Claim 1 as amended is directed to a method of inhibiting cytoskeletal rearrangement in a cell or cell fragment that comprises Fyb/SLAP and Ena/VASP proteins that form a complex. The Examiner agrees that Applicants are in possession of a method for inhibiting cytoskeletal rearrangement in a T cell or a platelet, a method of inhibiting a T cell response and a method for increasing platelet aggregation comprising contacting the T cell or platelet with an amount of a Fyb/SLAP complex inhibitor sufficient to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein wherein the Fyb/SLAP inhibitor is the EVH1 binding peptide FPPPP (SEQ ID NO:15). Applicants respectfully assert that the teaching

in the Specification and Examples indicate that Applicants were in possession of the claimed invention at the time of filing. Applicants stress that the claimed invention is not agents that can be used to inhibit cytoskeletal rearrangement, but rather methods of inhibiting cytoskeletal rearrangement in a cell or cell fragment that comprises Fyb/SLAP and Ena/VASP proteins that form a complex.

This distinction can be illustrated using the example of a method of treating a particular disease or disorder (e.g. cancer), which is inhibited by a class of drugs. Thus, in such an illustration, the claimed invention is the use of the class of drugs, not the individual drugs themselves, for use in the method of treating the disease. Similarly, in the claim at issue, Applicants claim a method of using a class of molecules, namely, Fyb/SLAP inhibitors to inhibit cytoskeletal rearrangement. The application provides, as described above, extensive teaching regarding how to identify, make, and test additional inhibitors of binding between Fyb/SLAP and Ena/VASP, but is not claiming these individual molecules as inhibitors. Thus, the Examiner's contention that a skilled artisan would be unable to envision all the contemplated inhibitor possibilities defined in the claims is not a valid basis for a written description rejection under 35 U.S.C. §112, first paragraph.

In view of the foregoing, Applicants respectfully request that the Examiner withdraw the rejections and act favorably upon the claims. If the Examiner requires clarification for any aspect of this response, or if prosecution can be expedited for any other reason, Applicants respectfully request that the Examiner contact the undersigned by telephone.

Respectfully submitted,



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## **Marked-Up Claims**

### **In the Claims**

1. (amended) A method for inhibiting cytoskeletal rearrangement in a cell or cell fragment that comprises Fyb/SLAP and Ena/VASP proteins that form a complex, comprising:

contacting the cell or cell fragment with an amount of a Fyb/SLAP complex inhibitor sufficient to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein.

2. (amended) The method of claim 1, wherein the Fyb/SLAP complex inhibitor binds to the EVH1 domain of the [the] Ena/VASP protein and inhibits binding of the Ena/VASP protein to a Fyb/SLAP protein.